CHAPTER

15

Organization of the Social Brain in Macaques and Humans

M.P. Noonan[a], *R.B. Mars*[a], *F.X. Neubert*, *B. Ahmed*, *J. Smith*, *K. Krug*, *J. Sallet*[a]

University of Oxford, Oxford, United Kingdom

Abstract

Human social life has changed dramatically in the past 100 years, as first advances in transport and later the Internet allowed us to interact with a much greater and more diverse group of people. As a result, even the term "social networks" has a profound new meaning in the 21st century. The human species is now more connected than ever, and we live in a world in which, for better or worse, we can communicate our thoughts and intentions to vast numbers of our conspecifics, instantly. Yet while the apps behind this revolution are upgraded each year, the neural hardware that supports social behavior evolves over millennia. This chapter will explore the evidence that our social brain and the brains of our less-technology-savvy cousins may be surprisingly similar.

INTRODUCTION

Human social life has changed dramatically in the past 100 years, as first advances in transport and later the Internet allowed us to interact with a much greater and more diverse group of people. As a result, even the term "social networks" has a profound new meaning in the 21st century. The human species is now more connected than ever, and we live in a world in which, for better or worse, we can communicate our thoughts and intentions to vast numbers of our conspecifics, instantly. Yet while the apps behind this revolution are upgraded each year, the neural hardware that supports social behavior evolves over millennia. This chapter will explore the evidence that our social brain and the brains of our less-technology-savvy cousins may be surprisingly similar.

Over the course of primate evolution better social abilities may have helped primates cooperate among conspecifics and together deal with predators and prey. The advanced social abilities of humans and other primates have been related to the large increase in brain size. The ratio of brain to body size is correlated with the number of individuals per social group, a variable that indexes the social complexity of a species' life [20]. While social behavior is intricate and multifaceted in nature, the size of the individual's social network is a useful and well-validated index [30,40] correlating with emotional intelligence and mentalizing abilities [85]. Social network size (SNS) reflects not only species differences but also differences in brain structure between individuals of the same species. In humans, correlates are reported between measures of SNS and gray matter (GM) volume in the amygdala and subregions of the temporal and frontal cortex [6,36,90]. Furthermore, blood oxygen level-dependent (BOLD) activity in these regions, measured while subjects made social closeness judgments, also correlates with individuals' SNS [90]. However, while neuroimaging studies in humans can allude to a network of brain regions involved in social cognition, they cannot reveal the directionality of structure–function relationships.

It is well established that the social environment during the time of development has a causal influence on behavior and brain structure [14]. We showed that changes in the social environment could cause changes in *adult* brains of nonhuman primates [74] as well. We manipulated the size of groups in which animals were housed and related this to changes in the size of

[a] Authors contributed equally to this work.

http://dx.doi.org/10.1016/B978-0-12-805308-9.00015-4

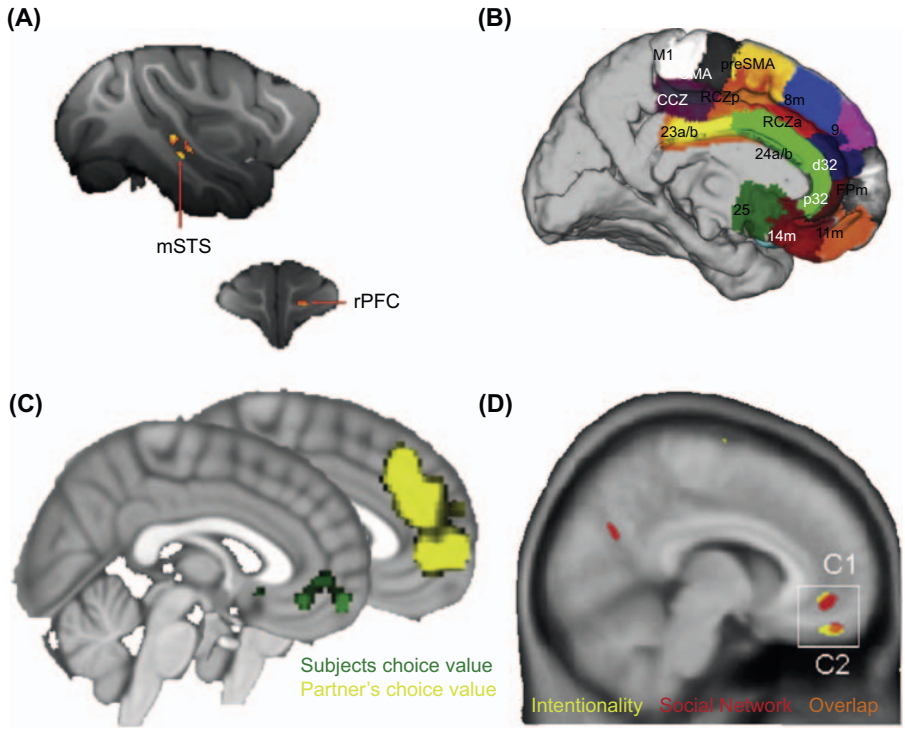

FIGURE 15.1 (A) Animals housed in large social groups had more gray matter volume in bilateral mid-superior temporal sulcus (mSTS) and rostral prefrontal cortex (rPFC). *(Adapted from Sallet J, Mars RB, Noonan MP, Andersson JL, O'Reilly JX, Jbabdi S, et al. Social network size affects neural circuits in macaques. Science 2011;334:697–700.)* (B) Subdivisions of the medial prefrontal cortex (MPFC). *(Adapted from Neubert FX, Mars RB, Sallet J, Rushworth MF. Connectivity reveals relationship of brain areas for reward-guided learning and decision-making in human and monkey frontal cortex. Proc Natl Acad Sci USA 2015;112:E2695–704.)* (C) MPFC blood oxygen level-dependent signal correlating modeled value of choices of a conspecific *(yellow)* and self-referential choices *(green)*. *(Adapted from Nicolle A, Klein-Flügge MC, Hunt LT, Vlaev I, Dolan RJ, Behrens TE. An agent independent axis for executed and modeled choice in medial prefrontal cortex. Neuron 2012;75:1114–21.)* (D) Individual differences in gray matter volume correlate with differences in mentalizing abilities and social network size. *(Adapted from Lewis PA, Rezaie R, Brown R, Roberts N, Dunbar RI. Ventromedial prefrontal volume predicts understanding of others and social network size. Neuroimage 2011;57:1624–29.)*

specific brain areas (Fig. 15.1A). Using the same imaging techniques and analysis methods as in the aforementioned human studies, correlations with SNS were observed in a limited number of brain regions that resemble the human regions, particularly in the temporal lobe and the medial prefrontal cortex (MPFC). Collectively this body of work raises the possibility that the extent of similarity between macaque and human social brains is underestimated. However, testing this proposition is difficult, as functional imaging studies aimed at comparing activity profiles of areas in the human and macaque brain are limited by the complexity of the tasks that macaques can perform in the scanner. This has led some (e.g., Ref. [42]) to question whether these debates can be resolved with behavioral experiments alone. We propose that interpretations of different patterns of activation elicited by social tasks, or different deficits induced by specific lesions, can be better understood by establishing the foundations of the social brain in the two species by directly comparing regional changes in structure and connectivity.

This chapter focuses on brain structure and functional connectivity of two key areas of the social brain: the MPFC and the temporal cortex (particularly the temporal parietal junction, TPJ). Our approach is based on a combination of magnetic resonance imaging (MRI)-based methods. Structural MRI allows us to identify brain regions where individual differences in GM volume correlate with indices of sociocognitive factors. By contrast, diffusion-weighted imaging (DWI) and resting state functional MRI (rsfMRI) can be used to determine the connectivity-based organization of regions of interest [47,57,58,75].

MEDIAL PREFRONTAL CORTEX

The MPFC is associated with the control of social behavior [17]. Case histories describe patients with damage to this region as having "acquired sociopathy," manifesting social impairments such as increases in the expression of socially inappropriate behavior and aggression, as well as the tendency to misinterpret

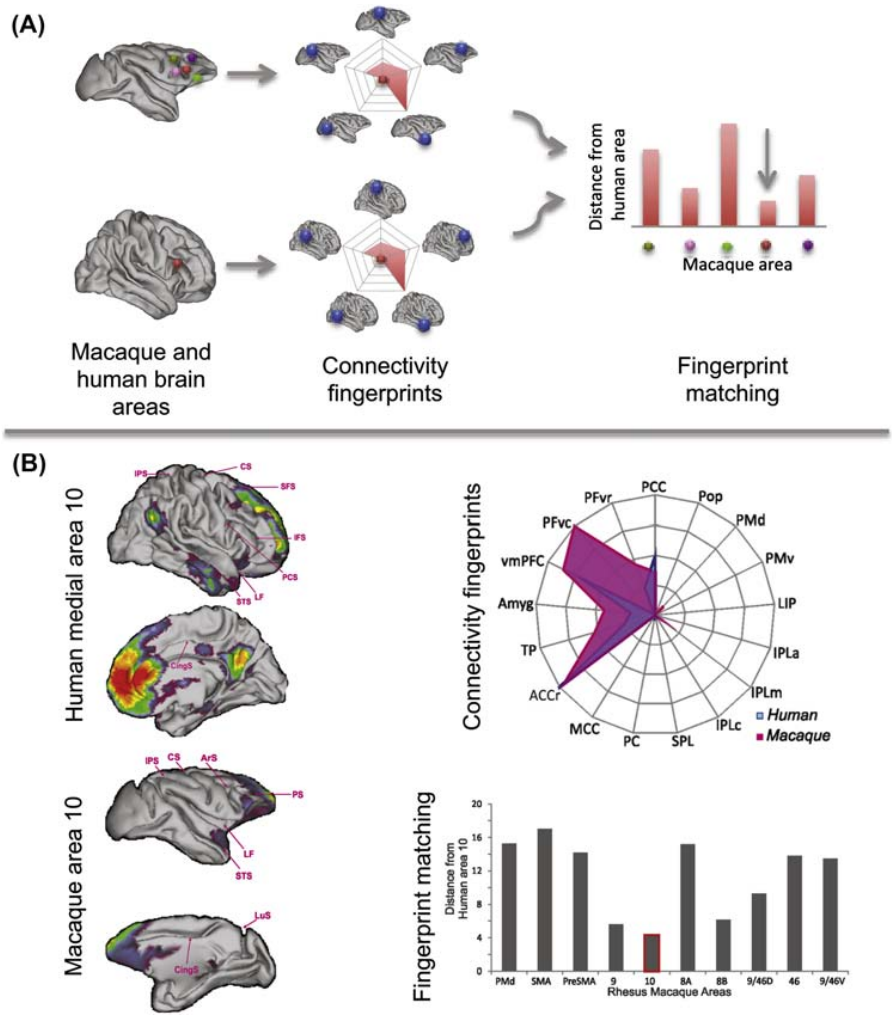

FIGURE 15.2 Connectivity-based comparison of human and macaque social areas in the medial prefrontal cortex. (A) Our strategy for identifying potential human/macaque homologs. We exploit the fact that each cortical area has a unique set of connections with the rest of the brain, termed its connectivity fingerprint (cf Ref. [63]). To identify the homolog of a human area (*red dot*) we chart its connectivity to a set of targets (*blue*) with known macaque homologies. We then define the connectivity fingerprint for a set of candidate areas in the macaque, with the same targets, and calculate a distance measure indicating how much each candidate's connectivity fingerprint differs from that of the human template. The macaque area with the smallest distance (indicated by the *arrow*) is the most likely candidate for between-species homology. *(Based on Mars RB, Verhagen L, Gladwin TE, Neubert FX, Sallet J, Rushworth MFS. Comparing brains by matching connectivity fingerprints (submitted for publication-b).)* (B) This approach was applied to area 10 in the medial frontal pole of the human brain. We determined its connectivity fingerprint (*top right*) using resting state fMRI (*top left*). The same was done for candidate areas in the macaque. The connectivity fingerprint of macaque area 10 best matched that of the human frontal pole, suggesting that even high-level areas share features between species. *(Adapted from Sallet J, Mars RB, Noonan MP, Neubert FX, Jbabdi S, O'Reilly JX, et al. The organization of dorsal frontal cortex in humans and macaques. J Neurosci 2013;33:12255–74.)*

other people's moods [31,32] and facial and vocal emotional expressions [28,32]. However, the MPFC is far from a unitary structure but refers to a collection of cytoarchitectonically distinct areas (Fig. 15.1B) with evidence that subregions support different computations [82]. A better understanding of the role of the MPFC in social cognition requires a careful examination of the subregions of this large cortical territory and an understanding of the distribution of sociocognitive function across these anatomical subregions (see Ref. [4,84]). This chapter will discuss which structural subdivisions might contribute to social cognition for future investigations.

In the human neuroimaging literature, the MPFC has become synonymous with "theory of mind," which is the act of attributing thoughts and feelings to others [1]. This skill is thought to be particularly well developed in the human [77]. The cytoarchitectonic areas 9 medial and 10 medial (or Frontopolar cortex, medial subdivisions (FPm)) are the two regions of the MPFC that are most often reported in fMRI studies in which subjects attempt to infer the intentions or beliefs of

others [1,59]. Other authors have emphasized a more ventral region, corresponding to cytoarchitectonic areas 11, 14, and p32 (Fig. 15.1C), as involved in mentalizing process [18,59]. Individual differences in GM volume in this ventromedial region also correlate with differences in mentalizing abilities, as do differences in SNS (Fig. 15.1D) [40,60].

Other parts of the MPFC have also been implicated in various aspects of social cognition. We find that GM volume in the dorsal anterior cingulate cortex (ACC) sulcus correlates with SNS both in humans and in monkeys [74,60]. Adjacent to it, the cortex of the cingulate gyrus is often shown to be recruited in tasks that require subjects to monitor the outcomes of other's decisions [2] or the reliability of information provided by a confederate [5]. An elegant study in monkeys by Rudebeck and colleagues [72] showed that macaques with anterior cingulate gyrus lesions (areas 24a,b and 32) lose interest in social stimuli. Intriguingly, in light of human neuroimaging results, lesions to the ventromedial cortex (area 11/14) do not induce the same social impairment [62].

A number of studies have investigated socioemotive functions in macaques [27,33] and the pattern is reminiscent of findings from human patients with MPFC lesions and human neuroimaging studies. However, when differences have been identified they have sometimes been thought to reflect uniquely human brain regions supporting uniquely human social behaviors [38,73]. Yet the uniqueness of human sociocognitive functions is still debated [29,42]. Direct between-species comparisons of function are challenging, but anatomical comparisons can provide the tools to establish homologies in the architecture of the social brain between the two species. Therefore, we have used different measures of connectivity to compare the organization of the MPFC between humans and macaques.

The connections of a brain region with the rest of the brain define a unique connectivity fingerprint [63], which can be used to compare regions across species ([51], see Fig. 15.2A [63], for description of technique). Using this technique, we found that the cortical areas composing human MPFC share similar connectivity patterns with areas of the macaque prefrontal cortex. Full regional comparisons are described in Refs. [75] and [58] but for the purpose of this chapter we focus on medial area 10(or FPm) to illustrate the principle of the comparative technique. We used diffusion MRI to identify the boundaries between cortical regions of the human MPFC and then used rsfMRI to compare the interactions or functional connectivity of these human areas with those of MPFC areas in the macaque. Analysis of the macaque data showed that area 10 is functionally coupled with other MPFC regions, with the temporal pole and cortex of the superior temporal sulcus (STS) as well as with posterior cingulate regions (see Fig. 15.2B). Classic tracing studies in monkeys have revealed similar patterns of connections [10,45,65]. Human medial area 10 matched this profile best, showing functional connectivity with the ventral PFC and anterior temporal and posterior cingulate areas.

As well as identifying structural homologs between species, it is informative to study how different brain regions relate to one another. For instance, visual areas are often described as organized hierarchically and their position in this hierarchy provides clues to their function. Cluster analysis of the connectivity patterns of MPFC areas suggest that these regions can be separated into distinct networks of regions [3,57]. Based on their connectivity pattern, the cingulate (area 24) and dorsomedial cortex (medial area 9) could be grouped, and the ventromedial regions clustered together (area 11 and 14). Note that there is no consensus regarding areas 32 and 10. Collectively, it appears that the relationship between MPFC regions, i.e., their place in the cortical hierarchy, is also similar between the two species. These network divisions may reflect and define their different functional roles in learning from others' actions and comparing social choices. For example, Nicolle and colleagues [59] report that when subjects are asked to make self-referential choices in an fMRI scanner, signals from ventromedial prefrontal areas (32/25, 14, and 10) correlate with the choice of the agent, whereas signals from the rostral dorsomedial PFC (10/9) reflected the modeled choices of a conspecific. However, when the subjects chose on behalf of their partner the roles of these regions were swapped (Fig. 15.1C).

Finally, there are similarities across species in terms of the whole-brain networks that these clusters participate in. There is a distinct common pattern of connections for areas 9, 10, 32, 11, and 14 within the MPFC and the rest of the brain. These regions are monosynaptically connected with other regions of the MPFC, the temporal pole, and posterior cingulate cortex (PCC) [93]. These areas are referred to as the default mode network (DMN), a resting state network typically isolated in task-negative contrasts, with more BOLD signal in these regions when subjects are resting between task blocks in the scanner (see Refs. [9,69]). The DMN arguably reflects the default mode of social animals' brain function, that of coordinating behavior within a social context, which grows in demand with larger SNSs [79]. Moreover, the typical pattern of DMN brain activity partly reflects that seen during tasks of social cognition, mentalizing, and autobiographical memory [48].

Beyond the species similarities detailed above, there are also distinct differences between human and macaque prefrontal–temporal brain connectivity. Whereas functional connections between temporal cortex and lateral prefrontal cortex are stronger in humans compared to

connections with MPFC in humans, the opposite pattern is observed in macaques [58]. Interestingly, reduced functional connectivity between frontal and temporal cortex has been observed in patients suffering from autism during the performance of a nonlinguistic theory of mind task, compared to a control group [35].

SUPERIOR TEMPORAL SULCUS AND TEMPORAL PARIETAL JUNCTION

As discussed previously, early human studies noted that GM in temporal cortex and the amygdala differed as a function of social complexity [7]. This modulation of amygdala GM by SNS was replicated in our macaque study [74] and subsequent human studies [36,40,60]. Interestingly, in macaques we found that amygdala GM was also associated with social status, an uncorrelated social variable [61]. However, the effect of SNS in amygdala GM was dorsal of the social status effect (see also Chapter 20 for the neural mechanisms underlying learning of social status in humans). This might reflect the diverse, dissociable nuclei of the amygdala, which have distinct connectivity profiles [24], and may support different roles in social cognition [6,56].

In the rest of the temporal cortex, there are many areas that respond to socially relevant stimuli—especially faces—and that correlate with SNS, in both humans and macaques. However, because the temporal cortex has undergone substantial reorganization since the last common ancestor [88], the identification of homologs between species is difficult. Some groups now use fMRI in awake macaque monkeys to give them face processing tasks similar to those given humans, to relate the different patches of activation in the two species, reporting potential homologs (e.g., Ref. [68]).

In the human brain, a prominent locus of socially related GM changes is in the posterior end of the superior temporal cortex, at the junction with the parietal and occipital cortex (cf Ref. [40]). It is known as the TPJ and has been shown to be active during higher order social reasoning tasks [78,82]. Indeed, TPJ GM changes are not correlated with SNS, but rather the ability to perform recursive social reasoning [40], which may enable complex chains of social inference ("I know that Mary thinks that John would like David to know that Gary wants…"). This ability may be unique, or at least more extensive, in humans [15]. Echoing this, the TPJ has been described as involved in "uniquely human social cognition" [77].

Despite the prominence of TPJ in the social literature, little is known about its precise anatomy. A number of authors have suggested that TPJ is not a separate region specifically involved in social cognition, but overlaps with another region also termed TPJ that is often reported when subjects reorient their attention in visual space. A number of studies either using metaanalyses of functional imaging studies [19] or testing both types of tasks in the same participants [54,81] could not resolve this controversy. However, despite similar loci of activity in the TPJ during processing of social information and reorienting of visual attention, the network of areas coactivated with TPJ in the two tasks is quite different, showing, among other regions, anterior MPFC during mentalizing task [11] but ventrolateral prefrontal cortex (VLPFC) during attentional reorienting [23]. This inspired Mars and colleagues to test the hypothesis that the large expanse of cortex termed "TPJ," as MPFC earlier, also consists of different subregions connected to different parts of cortex. Using a DWI tractography-based parcellation of TPJ, they indeed found that the posterior part of TPJ connects with nodes of the social brain, including anterior temporal cortex, PCC, and MPFC, whereas the anterior part of TPJ interacted with areas more often associated with attentional control, including the mid-cingulate cortex, anterior insula, and VLPFC [50]. Similar results were obtained by Bzdok et al. [12] using a connectivity-based parcellation of metaanalysis data.

Given the uncertainties of the anatomical properties of the TPJ and the fact that it is associated with activity during higher order social cognitive tasks that are thought to be uniquely human, the TPJ has not been linked to a monkey homolog. Because macaques cannot perform the same tasks that activate the human TPJ, a different approach was required. Taking an approach similar to that used when studying the human TPJ, Mars and colleagues [49] investigated whether TPJ can be matched to any macaque area based on anatomical grounds. They used a variant of the connectivity matching approach described earlier for frontal cortical areas and searched along the entire macaque brain for voxels that had a functional connectivity profile with the anterior, middle, and posterior cingulate cortex and the anterior insula/VLPFC similar to that of the human posterior TPJ. This approach identified the mid-STS (mSTS) as the macaque area with the most similar connectivity fingerprint (Fig. 15.3).

The area identified as anatomically similar to human TPJ was the same region that showed increased GM density in macaques living in larger social groups (see Ref. [74]). Interestingly, although identified from face processing in macaques, Perrett and colleagues [64] demonstrated that the cortex of the STS contains neurons that respond when a pair of eyes look in a particular location. If the eyes are not visible, then the neurons respond when the head is oriented in that direction. If the head is not visible, then the neurons respond to clues based on body posture. Thus, the mSTS seems to code for the focus of a conspecific's attention, rather than

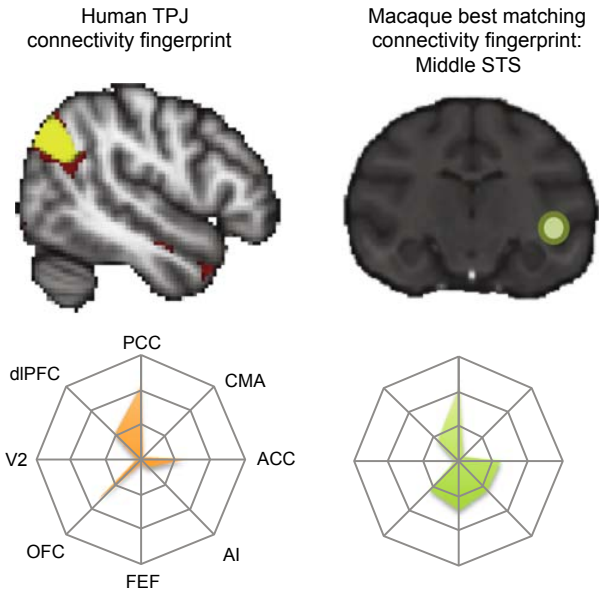

FIGURE 15.3 Similarity between human temporoparietal junction (TPJ) and an area in the macaque superior temporal sulcus (STS). The human TPJ (*top left*) is active during mentalizing tasks suggested to be uniquely human. Using the techniques outlined in Fig. 15.2, we sought to establish whether this region nevertheless had an anatomical homolog in the macaque. Using resting state fMRI, we determined the connectivity fingerprint of the human TPJ (*bottom left*) and searched for the best matching connectivity fingerprint from a set of 32 candidate areas along the macaque STS and inferior parietal cortex. An area in the middle part of the STS (*top right*) had the most similar connectivity fingerprint (*bottom right*). A control analysis searched across all voxels in the macaque temporoparietal cortex using a more restricted connectivity fingerprint, and identified the same areas. *Adapted from Mars RB, Sallet J, Neubert FX, Rushworth MF. Connectivity profiles reveal the relationship between brain areas for social cognition in human and monkey temporoparietal cortex. Proc Natl Acad Sci USA 2013;110:10806–11.*

facial identity; this being more specifically supported by the inferotemporal cortex face patches system [25]. Such an ability might be considered a prerequisite of our human mentalizing ability. Without knowing the focus of another's attention, it is impossible to learn about his or her beliefs and desires.

A SOCIAL BRAIN NETWORK

We have now described the organization of the MPFC and TPJ in the social brain, but these areas do not operate in isolation. An outstanding question is how they interact within a larger "social brain network" to produce behavior. It has been argued that pathologies in social cognition might be the result of dysfunctional interactions between brain regions [8]. Our own work using rsfMRI in macaques established that functional connectivity between these two nodes was causally related to SNS [74]. Within this premise we examined the contribution of the MPFC to larger distributed cortical networks, focusing on the DMN. In monkeys, and more recently in humans, we showed that changes in interareal couplings between the MPFC and the DMN relate to SNS [48,60].

While it is useful to characterize a network by its functional connectivity, the very nature of the method means we cannot address which anatomical white matter (WM) pathways support the transfer of neural information. Using DWI, a 2015 paper investigated the correlation between social network diversity and WM microstructural integrity in humans [55]. The results identify the corpus callosum, cingulum bundle, and hypothalamic pathways in a large group of subjects. Extending these findings, we found evidence that differences in the structural integrity of the cingulum bundle, extreme capsule (EmC), and arcuate fasciculus relate to SNS [60]. These WM pathways (Fig. 15.4) support frontal–temporal communication, and we have demonstrated with probabilistic tractography that the network connectedness of social GM nodes utilizes them.

An important next step will be to analyze the extent and connective profiles of WM bundles themselves. For example, whereas macaque tracing studies and human DWI studies show similar connections between superior temporal and lateral prefrontal cortex [26,66,80], the projection areas in the posterior part of the cortex may be unique to humans [22,86]. However, using DWI in both humans and macaques, Mars and colleagues [46] compared the course and cortical projections of WM fibers passing through the EmC. In both species, the EmC innervated a number of social brain regions in frontal cortical areas (areas 9 and 10) and superior temporal cortex, including the human TPJ. Notably, the authors observed some tracts that were not commonly reported in macaque studies. These tracts resemble those previously reported in the human, suggesting larger similarities between the species than originally thought.

The question remains from where the MPFC and mSTS receive their social information. The PCC and its associated neighbor, the precuneus (PCun), are prominent DMN nodes and often active in mentalizing and Theory of Mind (TOM) [44]. We observed GM changes as a function of SNS in the PCun/PCC [60]. The region is strongly connected to the MPFC and superior temporal cortex [9] and we report its interconnectedness to the social brain through some of the WM tracts found by Noonan et al. [60].

Gold standard tracing studies can further refine our understanding of the connectivity of these regions. For example, the macaque mSTS interconnects with adjacent cytoarchitectonic areas of the STS [83] (see also Fig. 15.5 [49]). It projects to the frontal lobes, including MPFC regions [41,45], but also to the inferior parietal lobe [71]. Note that projections to the frontal lobes seem to come

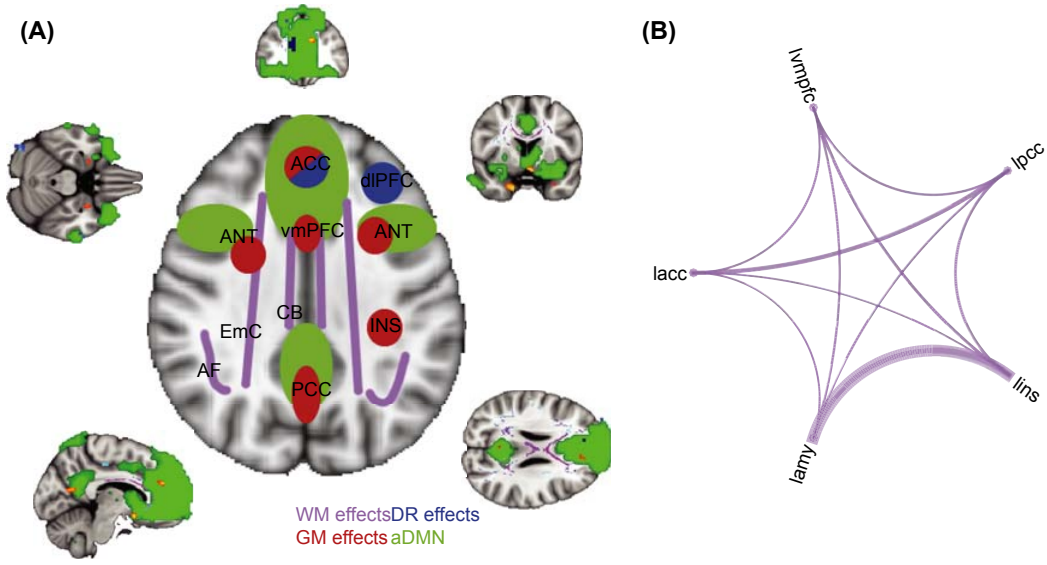

FIGURE 15.4 Summary figures of white matter (WM), gray matter (GM), and functional connectivity as a function of social network size (SNS) in humans. (A) Using diffusion-weighted imaging (DWI) we found that differences in the structural integrity of specific WM tracts—including cingulum bundle (CB), extreme capsule (EmC), arcuate fasciculus (AF), and corpus callosum—correlated with SNS measured over 30 days (*purple tracts*). Voxel-based morphology analysis demonstrated correlations between GM volume (*red-yellow*) and SNS in anterior cingulate cortex (ACC), ventromedial prefrontal cortex (vmPFC), and anterior temporal cortex. Finally, resting state fMRI demonstrated that the ACC and dorsolateral prefrontal cortex (dlPFC; *blue*) changed their functional contribution to the frontal component of the default mode network (aDMN; *green*) depending on SNS. (B) Probabilistic tractography seeded in the GM nodes, with the results of the DWI analysis used as waypoints, shows the proportion of tracts to reach each target seed in the left hemisphere. For each analysis the edges represent significant ($p < .05$) *t*-statistics against zero ($2.16 \leq t \leq 27.38$). *(Adapted from Noonan MP, Mars MB, Sallet J, Dunbar RIM, Fellows LK. The structural and functional brain networks that support human social networks (submitted for publication).)*

principally from the cortex on the dorsal bank of the STS. Fig. 15.5 illustrates the results of our work in which the retrograde tracer fluorogold was injected into the dorsal bank of the macaque mSTS. We show that this region receives monosynaptic input from both the dorsal visual area MT, linked to visual motion and depth perception [39], and the ventral visual pathway (area V4d), associated with object shape and color processing [70]. Altogether the connectivity of the macaque mSTS shows that this region is the nexus of several information streams.

SUMMARY AND PERSPECTIVES

We have described two brain regions associated with social cognition in both humans and macaques, the MPFC and the temporal cortex, in terms of their structure and their local/whole-brain connectivity. Despite the evolutionary expansion of the human brain and the increased complexity of our social networks, the results discussed in this chapter generally indicate that the brain networks supporting social cognition comprise similar building blocks in the human and in the macaque monkey. Although there are substantial differences in brain size and in the relative expansion of certain human brain areas (e.g., Ref. [88]), our research suggests principal similarities between the two social brains. However, humans display some social behaviors that are quite different from macaque behaviors. Tomasello and colleagues, for instance, have argued that humans are unique in the collaborative nature of their social interactions [87]. The question, then, is what changed to allow us to display these behaviors, if most of the neural building blocks are similar?

Several authors have proposed computational processes that our brain might be uniquely capable of implementing, or at least of implementing much better. As discussed, the human ability to infer the mental states of others far outstrips any such ability in the macaque, and may be due to our ability to process information recursively ("I think, that he thinks, that I think, that he thinks…") [15]. Performance of such recursive tasks is indeed associated with activity in some of the regions highlighted earlier, in particular in the MPFC [16]. The hypothesis described earlier, that the mSTS region tracking social signals is anatomically similar to the human TPJ region associated with attributing belief states to others might be seen in this light, as suggesting that we process similar sensory information about others in a way similar to that of macaques but to a deeper extent (cf Ref. [21]).

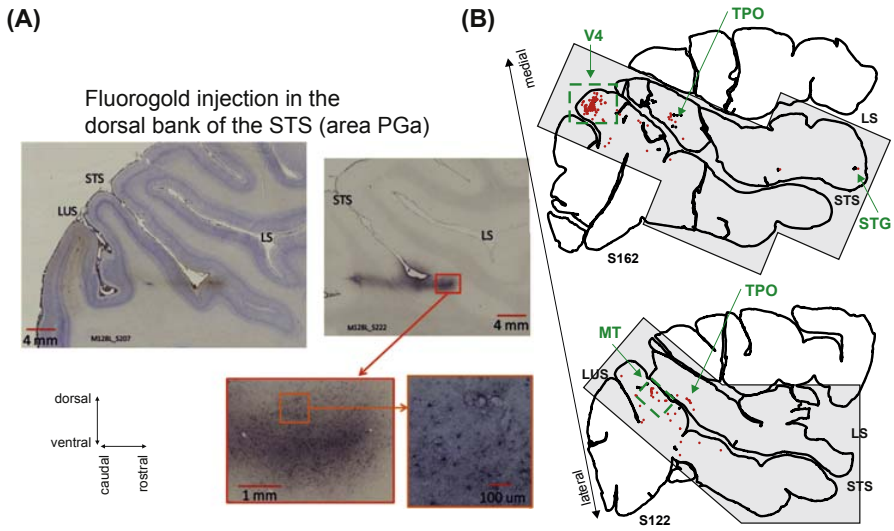

FIGURE 15.5 (A) Fluorogold, a retrograde tracer, was injected into the dorsal bank of a macaque's superior temporal sulcus (STS). Using Brainsight (Rogue Research, Montreal, QC, Canada), Mars et al. [49] showed that the injection site corresponded to monkey temporoparietal junction or mid-superior temporal sulcus. The panels illustrate the injection site and the stained cells at different levels of magnification on a parasagittal slice. (B) Parasagittal stained sections were examined under a light microscope using Neurolucida (MBF Bioscience, Williston, VT, USA). Fluorogold-stained cells (*red dots*) were found in dorsal V4 and middle temporal area (MT), indicating monosynaptic projections to the mSTS from both the dorsal (area MT) and the ventral visual pathways (area V4d). The *gray area* represents the area investigated for fluorogold-stained cells. *LS*, lateral sulcus; *LUS*, lunate sulcus.

While we have emphasized the similarities between species using MRI-based methods, we acknowledge that some disparity might be explained by methodological difference. For instance rsfMRI is usually recorded from humans at rest, yet macaques are usually scanned under anesthesia. General anesthesia is characterized by a decrease in spiking activity that results in a reduction in coupling between brain regions [89]. Therefore the difference between connectivity parameters, such as high-degree and betweenness centrality of the MPFC, in anesthetized macaques and awake humans should be considered carefully [53]. Despite this, our results continue to be upheld when examined with other techniques. For instance, the dissociation of human and macaque long-range connections to lateral prefrontal is mimicked in tracer and DWI data [10,67].

Finally, ending the discussion at the smallest scale, the cellular basis of experience-dependent plasticity following changes in the social environment inspires several hypotheses [34,52,76]. For instance blocking the synthesis of new neurons in subgranular and subventricular zones (neurons that will then integrate into the dentate gyrus of the hippocampus and the main olfactory bulb, respectively) had detrimental consequences for the social behavior of juvenile mice but it did not affect the social behavior of adult animals [92]. Increasing or decreasing the synaptic efficacy in the mouse MPFC markedly caused upward or downward change of the animal position in the dominance hierarchy [91] (see also Chapter 20). A study by Keifer et al. [37] showed that structural MRI changes were correlated with spine density. Findings that relate structural variations to differences in social behaviors may suggest that patients suffering from neurological and psychiatric disorders, as characterized by alteration of their social behaviors, will show corresponding changes in brain structure. Indeed changes in temporal and prefrontal cortex have also been reported in a monkey model of autism [43], whereas patients with Asperger syndrome have smaller prefrontal and temporal minicolumns than control subjects [13].

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